Title	A multi-center, prospective pilot study on safety and effectiveness of a healing ointment as a post-surgical care
Protocol number:	GLI.04.US.SL.017
Sponsor name and address:	Galderma Laboratories, L.P. 14501 North Freeway Fort Worth, TX 76177 USA
Test product:	Cetaphil® Healing Ointment
Investigator agreement:	I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described study in compliance with Good Clinical Practices (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, and all applicable regulatory requirements.
Principle Investigator:	
	Signature Date
Name:	Aaron Farberg, MD
Address:	Derm Texas 2110 Research Row Dallas, TX 75235 USA Telephone: (214) 845-6426 Legacy Dermatology 3140 Legacy Dr., #110 Frisco, TX 75034 USA Telephone: (972) 787-0010

A MULTI-CENTER, PROSPECTIVE PILOT STUDY ON SAFETY AND EFFECTIVENESS OF A HEALING OINTMENT AS A POST-SURGICAL CARE

APPROVAL SIGNATURE PAGE

Aaron Farberg, MD Principle Investigator Derm Texas and Legacy Dermatology	Date
Thu Q. Nguyen, PhD Project Manager Galderma Laboratories, L.P.	Date
Christine Emesiani, PharmD Medical Affairs Advisor, Consumer Galderma Laboratories, L.P.	Date
Matthew Meckfessel, PhD Director, Medical Affairs Galderma Laboratories, L.P.	Date

1. SYNOPSIS

Study Objective	To evaluate benefits of a Healing Ointment in skin improvement after dermatologic procedures
Methodology	Multi-center, prospective study
Number of Subjects at the end	20 subjects to complete
Study duration	28 days
Test product	Cetaphil® Healing Ointment
Conditions of use	Twice daily topical application and as needed
Study visits	Day 0, day 7 or 14, day 28
Specific Inclusion Criteria:	o **Demographics and study skin conditions** - Any race and ethnicity (to be recorded) - Fitzpatrick skin type (to be recorded) - Women or men - Age: 18 to 85 years old - Subject who undergo Mohs surgery, skin biopsy, excision on the head/neck or body o **Administrative** - Ability of giving consent for participation in the study - Agreement to adhere to the procedures and requirements of the study and to report to the institute on the day(s) and at the time(s) scheduled for the assessments.
Specific Exclusion Criteria:	- History of allergy or hypersensitivity to cosmetic ingredients - Pregnant, planning pregnancy during the course of the study or breastfeeding - Subject with a history of keloids or hypertrophic scars - Presence of tattoo and/or scar in the treatment area that in the investigator's opinion would interfere with study assessments - Subjects with history of or the presence of any skin condition/disease that might interfere with the diagnosis or

	evaluation of study parameters (i.e., atopic dermatitis, eczema, psoriasis, seborrheic dermatitis) at the discretion of the investigator. - Subjects with inability to comply with all study protocol restrictions and visits
Procedure	- Subjects will report to the site as screening visit, will be given an informed consent form, HIPAA form, photography release form, Code of Conduct form, and medical history form to complete. - Subjects will be screened on the basis of the selection criteria for study qualification. At day 0, investigator assessment (erythema, edema, scabbing/crusting, and overall wound appearance) and subjective tolerability assessment (burning, itching, pain) will be performed based on 0-4 analog scale. - Subjects will undergo the assigned surgical procedure. - After procedure, photography of the surgical site, investigator assessment and subjective tolerability will be performed, and investigator or staff will apply Healing Ointment immediately followed by a standard bandage. - Subjects will be instructed to apply the provided Healing Ointment to the wound at least twice daily and reapply as needed. - Subjects to return to the site at day 7 (± 2 days for head/neck group) or day 14 (± 2 days for body group), and day 28 post-treatment (± 3 days) for follow-ups. - For each follow-up visit, investigator will perform objective assessment and photography. Subjects will perform additional subjective tolerability assessment and self-assessment questionnaire.
Statistical analysis	Clinical grading and questionnaire.

2. TABLE OF CONTENTS

3. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse Event
°C	Degrees Celsius
CRF	Case Report Form
etc.	et cetera
e.g.	for example (Latin; exempla gratia)
°F	Degrees Fahrenheit
GCP	Good Clinical Practice
HA	Hyaluronic Acid
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICF	Informed Consent Form
ICH	International Conference on Harmonization
ICT	Information and communication technologies
i.e.	that is (Latin; id est)
IEC	Independent Ethics Committee
IRB	Institutional Review Board
N or n	Number
%	percent
SAE	Serious Adverse Event
SD	Standard deviation
SOP	Standard Operating Procedure

4. BACKGROUND AND RATIONALE

Post-surgical wound care is imperative to promote rapid healing without complications. The key principle of wound management is to create an occlusive, clean, and moist environment at the wound site to reduce the possibility of infection and facilitate the wound healing phases.[1] Two (2) common topical applications to achieve this optimal condition are topical antibiotics and over-the-counter (OTC) petrolatum-based ointments. While both methods have comparable wound-healing properties, topical antibiotics have been shown to potentially cause drug resistance or allergic contact dermatitis.[2-4] For this, dermatologists often opt for petrolatum-based ointment application for wound healing.

Cetaphil® Healing Ointment (Galderma, Fort Worth, TX) is an OTC skin protectant that contains 71.5% petrolatum, shea butter to soften, smooth and hydrate, as well as vitamin E to help support moisture barrier function. The Healing Ointment has been clinically proven to hydrate the skin's natural barrier for 48 hours while quickly protecting and healing dry, irritated skin for visible improvement in 1 week. The product is also hypoallergenic, non-comedogenic, gentle on sensitive skin and accepted by the National Eczema Association. These beneficial properties make Cetaphil® Healing Ointment an ideal candidate as a post-surgical wound care. This study is to investigate safety and efficacy of Cetaphil® Healing Ointment in wound healing after dermatologic procedures.

5. STUDY OBJECTIVE AND CLINICAL HYPOTHESIS

5.1 Study Objective

To evaluate safety and efficacy of a Healing Ointment in skin improvement after dermatologic procedures such as Mohs surgery, skin biopsy, excision on the head/neck or body.

5.2 Clinical Hypothesis

The Healing Ointment, consisting of skin protectant petrolatum and other beneficial ingredients, will be able to protect and promote healing of the wound site post-surgery.

6. SELECTION AND DISPOSITION OF STUDY POPULATION

6.1 Number of Subjects

A maximum 20 subjects to complete the study, in which 10 subjects with dermatologic procedure on the head/neck and 10 subjects with dermatologic procedure on the body.

6.2 Study Population Characteristics

Males and females who undergo Mohs surgery, skin biopsy, or excision on the head/neck or body (inclusive and a good ratio of each surgical type within the study panel).

6.3 Inclusion Criteria

1. Subjects of 18 to 85 years of age.
2. Subjects with a clinical diagnosis that requires invasive procedure such as Mohs surgery, skin biopsy, excision on the head/neck or body.
3. Subjects of any gender.
4. Subjects of any race and ethnicity.

5. Subjects of any Fitzpatrick skin type.
6. Subjects who are able and willing to provide written informed consent prior to any study related procedures.
7. Subjects who agree to be photographed at each visit.
8. Subjects apprised of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and applicable state Bill of Rights.
9. Subjects who agree to adhere to the procedures and requirements of the study, to report to the institute on the day(s) and at the time(s) scheduled for the assessments, and to complete all required visits.

6.4 Exclusion Criteria

1. Subjects with history of allergy or hypersensitivity to cosmetic ingredients or skincare products.
2. Subjects who are pregnant or breast-feeding, or who plan to become pregnant or breast feed during the course of the trial.
3. Subjects with a history of keloid or hypertrophic scars.
4. Subjects with presence of tattoo and/or scar in the treatment area that in the investigator's opinion would interfere with study assessments.
5. Subjects with any diseases, condition or presentation that may, in the opinion of the investigator, may put the subject at risk, may confound study results, or may interfere with participation in the study.
6. Subject with inability to comply with all study protocol restrictions and visits.
7. Subjects that are relatives of the investigator or are themselves or a relative of any study staff or any Galderma employee.
8. Subjects who have participated in an investigational study within 30 days of enrollment; participated in biologic investigational studies within 90 days of enrollment, or subjects planning to participate in any other interventional clinical research study while enrolled in this trial.
9. Subjects with known immunosuppression or immunosuppressive illness.
10. Subjects with uncontrolled diabetes or autoimmune disorders.
11. Use of concomitant medications that have the potential to prolong bleeding times such as anticoagulants or inhibitors of platelet aggregation (e.g., aspirin or other nonsteroidal anti-inflammatory drugs, Omega 3 or Vitamin E), within 14 days prior to surgical procedures. Omega 3 and Vitamin E were acceptable only as part of a standard multivitamin formulation.

6.5 Concomitant Therapies

All treatments and therapies used 30 days prior to enrollment (visit 1/screening) or 90 days prior to enrollment for biologics and all treatments or therapies used during the course of the study must be recorded in the Case Report Form (CRF) or electronic Case Report Form (eCRF).

6.5.1. Authorized Therapies

Unless listed under the exclusion criteria (Section 6.4) or in Prohibited Therapies (Section 6.5.2), other therapies to treat ongoing conditions are authorized.

6.5.2. Prohibited Therapies

None other than as specified in the Inclusion/Exclusion criteria.

The decision to administer a prohibited medication/treatment should be made with the safety of the subject being the primary consideration. Whenever possible, Galderma Laboratories, L.P. should be notified before the prohibited medication/treatment is administered to discuss possible alternatives.

If a subject receives prohibited therapy during the study, the subject may be allowed (at the discretion of the investigator / Galderma Laboratories, L.P.) to continue in the study for safety evaluation purposes, only.

7. STUDY TREATMENT

The term “study treatment” refers to the study product (see Section 7.1)

7.1 Product Identification and Use

Study product: Cetaphil® Healing Ointment	
Form	Opaque ointment
Mode of Administration	Topical
Formula code	1748
Formula number	B50H48
Lot numbers	0281N14C
Storage and Handling	The product is to be stored under controlled room temperature conditions 20°C to 25°C (68°F to 77°F), protected from freezing and sunlight.

The ingredient list of the study product is included in Appendix I.

7.2 Additional Products and Materials

The Sponsor will only provide Cetaphil® Healing Ointment for the study. The study overhead will cover any additional materials or supplies.

7.3 Study Product Accountability

Upon receipt of the study products, the investigator or designee will conduct an inventory. In accordance with federal regulations, the investigator must agree to keep all test articles in a secure location with restricted access. Designated study personnel will provide the test article to the subjects in accordance with the protocol.

During the study, the investigator must maintain records of study treatment dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of clinical supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. At the conclusion of the study, the investigator will be responsible for returning all unused study product (i.e., Cetaphil® Healing Ointment) unless otherwise instructed by the Sponsor. Shipping label and cost will be provided to the investigator by the Sponsor.

7.4 Method of Treatment Assignment

Subjects will be numbered sequentially in the order in which they qualify for entry into the study.

7.5 Treatment Product Dispensing

All treatment products will be administered only to subjects enrolled in the study, at no cost to subjects, and in accordance with the conditions specified in the protocol.

7.6 Treatments Compliance

Subjects will complete a daily diary, recording treatment product applications and comment during the study. Treatment product and diaries will be dispensed to subjects at Day 0 and reviewed for compliance at Day 28 visit. Treatment product will be visually inspected and weighed prior to distribution at Day 0 and at Day 28. Subjects will be instructed to return the treatment product and daily diary at Day 28 visit. If subjects do not return their treatment product or diary at the end of the study, a verbal confirmation will be obtained for usage compliance, and it will be documented as a note to file.

Any suspected noncompliance with the treatment product or study instructions will be addressed by the Investigator or clinic staff. The Investigator will determine whether a subject's noncompliance will affect the study outcome and whether the data should be excluded from statistical analyses.

8. TREATMENT OF SUBJECTS

8.1 Informed Consent Form

An IRB-approved informed consent form (ICF), consistent with the requirements in 21 Code of Federal Regulations (CFR) 50.25, will be given to each prospective subject. Prospective subjects will be given as much time as needed to read the ICF and will have the opportunity to have any study-related questions answered to their satisfaction prior to signing the ICF. If further questions exist, prospective subjects will be given sufficient time during the first visit to have questions regarding the study and/or the ICF answered by the Investigator, or clinic staff prior to signing.

8.2 Subject Identification

Enrolled subjects will be assigned a 3-digit subject number when used in conjunction with their initials. This will uniquely identify every subject on the study. These numbers will remain with the subjects throughout the study and should be used in all references to the individual in this study. No subject number will be reassigned once the study begins.

8.3 Subject Instructions

Subjects will be provided with the following instruction to follow upon the surgical procedure completion:

8.3.1. Post-procedure Instructions

- Keep procedure/surgical bandage in place for 36-48 hours. Remove and clean incision with warm soapy water or half-strength peroxide as needed. Do not submerge in water. Pat dry with clean towel. Limit strenuous activity.

8.3.2. Treatment Product Usage Instruction:

- Apply the provided treatment product liberally to the surgical site at least twice a day. Reapply as needed throughout the day. Apply bandage as needed.

8.3.3. Subject Instructions for Study Visits

- Bring the treatment product and daily diary with you to every visit.

8.3.4. General Study Instructions

- Avoid extended periods of sun exposure for the duration of the study.
- Do not use any topical products (except sunscreen as needed) on the surgical site other than the provided treatment product for the duration of the study.

9. STUDY PROCEDURES

The table below represents a summary of the study procedures and evaluation schedule:

1. Visit 1 – Screening
2. Visit 2 – Baseline/Day 0 (surgical procedure)
3. Visit 3 – Day 7 (for head/neck group) or Day 14 (for body group)
4. Visit 4 – Day 28

Test design / flow chart	Visit 1	Visit 2		Visit 3	Visit 4
	Screening	Baseline Day 0 Pre-procedure	Baseline Day 0 Post-procedure	Day 7 or Day 14	Day 28
ICF and qualification/enrollment	X				
Photo consent	X				
Demographics/Med History	X				
Concomitant Meds.	X				
Inclusion and exclusion criteria	X				
CRF		X	X	X	X
Investigator grading		X	X	X	X
Subjective tolerability grading		X	X	X	X
Standardized photography		X	X	X	X
Self-assessment questionnaire				X	X
AE reporting			X	X	X
Treatment product		W	D	W	C/W
Daily diaries			D	C/D	C

For treatment product and/or daily diaries: W = Weigh, D = Distribute, C = Collect

9.1 Visits and Examinations

9.1.1. Visit 1 (Screening)

1. Subjects will report to the clinic for screening to determine if they are eligible to be in the study.
2. Prior to beginning of any study related activities, subjects will be informed about the purpose and nature of the study, the expected post-procedure events, and the potential risks involved with the surgical procedure and treatment product.
3. Subjects will be given an ICF, HIPAA form, and photography release form to read.
4. Once subjects have completed reading, they will be interviewed to ensure their understanding of the aforementioned forms and be given the opportunity to ask any study related questions.
5. Subjects who agree to sign the aforementioned forms will be asked to complete a demographic information, medical history form, and concomitant medication form. Subjects declining to sign any of the forms will be dismissed from the study.
6. Subjects will be screened and qualified on the basis of the subject inclusion and exclusion criteria. Subjects failing to meet criteria will be dismissed from the study.

9.1.2. Visit 2 (Baseline/Day 0 – Surgical procedure)

1. Investigator or clinic staff will ask the subjects if they have experienced any changes in their health since the previous visit.
2. Before the surgical procedure, the assessments below will be completed:
    a. Clinical grading by Investigator as described in section 10.1
    b. Tolerability assessment by the subjects as described in section.
3. The surgical area will be assessed and prepped for the procedures, followed by procedure execution by Investigator.
4. After the surgical procedure, the assessments below will be completed:
    a. Standardized photography as described in section 10.3
    b. Clinical grading by Investigator as described in section 10.1
    c. Tolerability assessment by the subjects as described in section 10.2
5. Investigator or clinic staff will apply the treatment product to the surgical site followed by standard bandage.
6. Subjects will be given the treatment product with instruction of application, a diary to record usage of the treatment product, and when to contact the Investigator in case of emerging AEs.
7. Subjects will be scheduled for a follow-up visit at Day 7 or 14 (±2 days) and dismissed from the Clinic.

9.1.3. Visit 3 (Day 7 or Day 14 ±2 days)

1. Clinic staff or Investigator will record any AEs that are observed or reported.
2. The surgical site will be assessed in the following:
    a. Clinical grading by Investigator as described in section 10.1
    b. Tolerability assessment by the subjects as described in section 10.2
    c. Standardized photography as described in section 10.3
    d. Self-assessment questionnaire as described in section 10.4
3. Clinic staff or Investigator will collect and review the treatment product and diary for compliance purpose.

4. Subjects will be scheduled for a follow-up visit at Day 28 (±3 days) and dismissed from the Clinic.

9.1.4. Visit 4 (Day 28 ±3 days)

1. Clinic staff or Investigator will record any AEs that are observed or reported.
2. The surgical site will be assessed in the following:
    a. Clinical grading by Investigator as described in section 10.1
    b. Tolerability assessment by the subjects as described in section 10.2
    c. Standardized photography as described in section 10.3
    d. Self-assessment questionnaire as described in section 10.4
3. Clinic staff or Investigator will collect and review the treatment product and diary for compliance purpose.
4. Once completed, subjects will be dismissed from the Clinic.

9.2 Discontinued Subjects

Any subject is free to discontinue his/her participation in this study at any time and for whatever reason, specified or unspecified, and without prejudice.

Investigator may decide to discontinue a subject from the study for safety reasons or when it is in the best interest of the subject. Galderma Laboratories, L.P. may also decide to prematurely terminate or suspend the study or the participation of a subject in the study. All data gathered on the subject prior to termination should be made available to Galderma Laboratories, L.P.

Criteria for the discontinuation of a subject during the study will include the following:

- Adverse Event
- Lack of Efficacy
- Pregnancy
- Subject Request
- Protocol Violation
- Lost to Follow-up
- Any unmanageable factor, in the Investigator's opinion, that may significantly interfere with the protocol or interpretation of results.

10. STUDY ASSESSMENTS

All data and images taken from the study will be saved and shared to the Sponsor via a data-protected platform.

10.1 Clinical Grading by Investigator

Investigator will perform clinical grading at the surgical site on each subject at baseline (pre- and post-procedure), day 7/14, and day 28. Investigator will grade the severity of wound parameters based on a visual analog scale, described in the table below (for erythema, edema, overall wound appearance, half-point scores can be used as necessary to better describe the condition):

Parameters	Score 0	Score 1	Score 2	Score 3
Erythema	None/absent	Mild	Moderate	Severe

Edema	None/absent	Mild	Moderate	Severe
Overall wound appearance	Excellent (absent of wound)	Good (slightly visible wound)	Fair (moderately visible wound)	Poor (marked visible wound)

Parameters	Score 0	Score 1	Score 2	Score 3	Score 4
Scabbing/crusting	None	Slight (up to 30%)	Moderate (31-60%)	Extensive (61-90%)	Almost complete or complete (91-100%)

10.2 Tolerability Assessments

Tolerability assessments will be performed by subjects at the surgical site at baseline (pre- and post-procedure), day 7/14, and day 28. Subjects will grade the degree of irritation parameters that they experience based on a 4-point analog scale, described in the table below (with half-point scores used as necessary to better describe the clinical condition):

Parameters	Score 0	Score 1	Score 2	Score 3
Burning	None	Mild	Moderate	Severe
Itching	None	Mild	Moderate	Severe
Pain	None	Mild	Moderate	Severe

10.3 Standardized Photography

Standardized digital photography of the surgical site will be taken at baseline (pre- and post-procedure), day 7/14, and day 28.

The following guidelines of digital photography are followed:

- Surgical site position is the same in before and after photos
- Same lighting conditions are used and the distance from the camera is same for both before and after photos
- Same room and white background are used for both before and after photos
- Clean skin
- Avoid any object that could interfere with the images such as hair, jewelry, etc.

A total of 4 digital images will be taken of each subject's surgical site using a Canon EOS Rebel T5 digital camera (Canon Inc., Taiwan) under the standard lighting condition.

10.4 Self-Assessment Questionnaire

Subjects will complete self-assessment questionnaire at day 7/14 and day 28. See Appendix II: Self-assessment questionnaire.

11. STATISTICAL ANALYSIS

A descriptive statistical summary will be provided for clinical grading and tolerability assessments. The descriptive summery will be performed for each parameter, including N, mean, median, standard deviations, minimum, and maximum of values at all applicable time points.

Mean of the change from baseline (pre-procedure) will be estimated at applicable post-baseline time point. The null hypothesis, that the mean change from baseline (pre-procedure) is zero, will be tested using methods described in the Statistical Analysis Plan table.

The following will be calculated and reported for each evaluation parameter at applicable post-baseline (pre-procedure) time point:

$$\text{Percent mean change from baseline} = \frac{(\text{postprocedure or visit mean score} - \text{baseline preprocedure mean score})}{\text{baseline preprocedure mean score}} \times 100$$

$$\text{Percent of subjects improved/worsened} = \frac{(\text{number of subjects improved/worsened from baseline preprocedure})}{\text{total number of subjects}} \times 100$$

Questionnaires will be tabulated, and the percentage of all response options (favorable and unfavorable) will be reported for each question and each timepoint.

Statistical Analysis Plan

Evaluation	Change from Baseline Pre-Procedure	Notes/Interpretation
Clinical grading	Paired t-test; If normality fails, a Wilcoxon signed-rank test will be used.	A decrease in scores indicates an improvement
Tolerability assessment	Paired t-test; If normality fails, a Wilcoxon signed-rank test will be used.	A decrease in scores or lack of significant increase indicates tolerability/safety of the treatment product
Self-assessment questionnaire	N/A	Percentage of favorable and unfavorable responses will be provided for each question.

All statistical tests will be 2-sided at significance level alpha = 0.05 unless specified otherwise. *P* values will be reported to 3 decimal places.

12. ADVERSE EVENTS

Throughout the course of the study, all adverse events will be monitored and reported on an adverse event CRF/eCRF without omitting any requested and known information. When AEs occur, the main concern is the safety of the study subjects. At time of the informed consent signature, each subject must be given the name and phone number of investigational site personnel for reporting AEs and medical emergencies.

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the investigator should inquire about AEs by asking the standard questions:

- "Have you had any health problems since your last study visit?"
- "Have there been any changes in the medicines you take since your last study visit?"

AEs should be reported for any clinically relevant change, as determined by the Investigator, in concomitant medication(s) that is the result of an untoward (unfavorable and unintended) change from baseline in a subject's medical health following exposure to the study treatment.

Changes from baseline in any protocol-specific parameter evaluated during the study are to be reviewed by the Investigator. In addition, the subject's responses to any questionnaire utilized during the study are to be reviewed by the investigator. Any untoward (unfavorable and unintended) change from baseline in a protocol-specific parameter or question response that is clinically relevant, in the opinion of the investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

12.1 Definitions

12.1.1. Adverse Events (AE)

An adverse event (AE) is defined as any untoward medical occurrence in a subject taking part in the clinical study, and which does not necessarily require a causal relationship with the investigational product and/or a clinical trial procedure.

An AE can be any unfavourable and unintended sign (including an abnormal laboratory value), symptom, or disease temporally associated with the use of the investigational product, whether or not related to this product.

When an AE has a likely or very likely causal relationship with the investigational product and/or a clinical trial procedure, it is named undesirable effect or related AE (see Section 3).

12.1.2. Local tolerability signs and symptoms (only applicable for cosmetic safety studies)

In cosmetic studies, local skin tolerability includes some expected functional and/or physical signs on the application area, observed by the Investigator or reported by the subjects (see Appendix). Those signs are collected in the final report based on scales or a diary. If the severity of a local skin tolerability sign or symptom, is such that the product application is permanently discontinued and/or a corrective concomitant treatment (except moisturizer or emollient) is prescribed, it is recorded as an undesirable effect (related AE).

12.1.3. Serious Adverse Events (SAE) and serious undesirable effect/related SAE

A Serious Adverse Event (SAE) is any adverse event which results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Notes:

The term "immediate vital risk" refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it was more severe.

Inpatient hospitalization is considered to have occurred if the subject has had to stay for a night at the hospital. Hospitalization solely for the purpose of a diagnostic test (even if related to an AE), elective hospitalization for an intervention that was already planned before subject enrolment in the clinical trial, admission to a day-care facility, social admission (e.g., if the subject has no place to sleep), or administrative admission (e.g., for a yearly examination) should not be considered as a SAE.

A serious undesirable effect/related SAE is defined as any SAE which the Investigator classifies as having a reasonable possibility for a causal relationship with the investigational product and/or the clinical trial procedure.

12.2 Severity Assessment

For all AEs occurring during the clinical trial, the Investigator is to classify and report the intensity of AEs using the following definitions as a guideline:

- Mild: awareness of signs and symptoms, but easily tolerated
- Moderate: discomfort, enough to cause interference with usual activity
- Severe: incapacitating, with inability to work or perform usual activity.

12.3 Causality Assessment

The Investigator is to assess the causal relationship (causality) between an adverse event and the investigational product and/or the clinical trial procedure according to the following definitions (Decision of 25 November 2013 on Guideline on Annex I to Regulation (EC) No 1223/2009 (2013/674/EU) - Causality assessment of undesirable effect caused by cosmetic products):

- Very likely
- Likely
- Not clearly attributable
- Unlikely
- Excluded

Medical judgment should be used to determine the relationship, considering all relevant factors including the pattern of reaction, temporal relationships, positive de-challenge or re-challenge, relevant medical history, and confounding factors such as co-medication or concurrent diseases.

12.4 Collection, Management and Reporting Procedures

The period of collection of adverse events starts from the time of signature of the Informed Consent Form (ICF) by the subject *(and/or, for subjects who are minor, by the parents/legal representatives)* until the end of the subject's participation in the clinical study.

If a Serious Adverse Event (SAE) is on-going at the final clinical trial visit, it should be followed by the Investigator until it has resolved or has reached a stable condition.

After the subject completes the clinical study, the Investigator should also inform the Sponsor (see Sponsor's contact details below) if he/she becomes aware of an SAE involving a subject who has participated in the clinical study.

At each post-enrollment visit, the Investigator will question the subject about AEs using an open non-persuasive question to elicit reporting of AEs, for example "*Have you noticed any change in your health since the last visit?*" Direct questioning and examination will be performed when appropriate.

The Investigator will obtain and maintain in the subject's files all pertinent medical records, and (if applicable) information and medical judgment from colleagues who assisted in the treatment and follow-up of the subject. If necessary, the Investigator will contact the subject's personal physician or hospital staff to obtain further details.

As a minimum, Investigators are requested to report in the Case Report Form (CRF) and in the report all related adverse events (i.e. undesirable effects) and all Serious Adverse Events, whether related or not.

12.4.1. Management and reporting procedures for undesirable effects (i.e. related adverse events

Undesirable effects should be recorded in the CRF and summarized in the report in a summary table with at minimum the subject number, AE number, AE diagnosis or signs and symptoms, location, date of onset, seriousness, severity, action taken, relationship, date of resolution and concomitant treatment associated as well as a detailed narrative of the event.

In addition, based on his/her medical judgment, the Investigator will assess whether an undesirable effect requires immediate (i.e. within 24 hours) reporting to the Sponsor. In such cases, the summary table will be sent to the Sponsor, along with the AE narrative and any other relevant information (concomitant treatments, product weighing, …).

All undesirable effects should be appropriately documented, i.e. any relevant information such as demographics, medical history and concomitant therapies should be recorded in the CRF.

The Investigator is to monitor and record the progress of the adverse effect until the last subject's study visit.

The Investigator is to update the AE narrative as appropriate, each time follow-up information is collected and when the final outcome of the adverse effect is known.

12.4.2. Management and reporting procedures for Serious Adverse Events

The Investigator is to take the following steps:

1. Take prompt and appropriate medical action, if necessary. The safety of clinical trial subjects is the first priority
2. Ensure the AE is classified as an SAE. Immediately inform the Sponsor's representative of the event by email or fax (see contact details below) and discuss further actions to be taken:

   e-mail: pharmacovigilance@galderma.com
3. Complete the Serious Adverse Event (SAE) form provided by the Sponsor's representative **Within 24 hours**, fax or send by e-mail **to the Sponsor's representative** the completed SAE form, accompanied any other relevant information (e.g. test results or medical records).
4. Monitor, record and send to Sponsor's representative the progress of the event until it resolves or reaches a stable outcome, with or without sequelae (send the updated SAE form with follow-up information and any other relevant information to Sponsor's representative).
5. Obtain and maintain in the subject's file all pertinent medical records, information, and medical judgments from colleagues who assisted in the treatment and follow-up of the

subject. If necessary, contact the subject's personal physician or hospital staff to obtain further details.

6. If applicable, comply with the regulatory requirement(s) related to the reporting of SAEs to the Institutional Review Board (IRB) / Independent Ethics Committee (IEC).

12.5 Pregnancy

Pregnancy itself is not to be considered as an adverse event. If a pregnancy occurs during the clinical trial, **the product application should be stopped immediately**, the subject should be withdrawn from the clinical study and Sponsor's representative (see Sponsor's contact details above) should be informed **within 24 hours.**

Pregnancy must be recorded as a reason for discontinuation in the exit form of the CRF.

No specific follow-up of pregnancy is required, except if it is a regulatory requirement in the country(ies) where the clinical trial is conducted.

12.6 Process for Suspected Allergic Reactions

In case of a positive reaction (suspicion of allergy) in the clinical study, the Investigator will inform the Sponsor if the reaction occurs with the Sponsor's company product(s) following the procedure below. The Investigator will also inform if products other than the Sponsor's product(s) were concomitantly tested in the clinical trial, and if there were positive reaction(s) for these other products.

- Stop the investigational product.
- Take a picture of the affected area and the surrounding skin.
- Report the event by email **within 24 hours** to the Sponsor's representative (see Sponsor's contact details above). The Sponsor will then contact you to explain the general procedure to be followed.
- Follow the procedure detailed below:
    1. After all signs and symptoms of the event have resolved and after a minimum of at least two weeks from last dose application perform a re-challenge test with the assigned study product
    2. Ensure the subject has not been under any treatment with corticosteroids or antihistaminics within the week before testing
    3. Ensure that the skin on the back has not been irradiated by the sun or artificial ultraviolet sources within the week before testing
    4. Apply an appropriate quantity of the study product to fill in the cupule of the test chamber and then to the upper part of the back skin (or the inner forearm if more appropriate) either at right or left from the central line. If no test chamber is available on site, patch test units will be provided by the Sponsor. The use of semi-occlusive conditions can be preferred depending on the irritant potential of the study product and the intensity of the reaction which was reported. The method to be used should be discussed with the Sponsor.

    Choose a skin site that was not previously involved in the inflammatory skin reaction. Cover it for 48 hours with a hypoallergenic tape

    5. Subject should be informed about avoiding exercise, showers, etc. to keep the test system dry

6. After 48 hours, remove the tests and evaluate the site reactions:

- 30 minutes after patch test removal (1st reading),
- 48 hours after patch removal (2nd reading).
- 72 or 96 hours after patch removal (3rd reading).

Pictures of the tested areas will be taken systematically at each reading and properly documented

7. Use the following scoring system (International Contact Dermatitis Research Group) at each reading:

Score	**Morphology**	**Interpretation**
-	No reaction	Negative
?	Erythema only, no infiltration	Doubtful reaction
+	Erythema, infiltration, possibly discrete papules	Weak positive reaction
++	Erythema, infiltration, papules, vesicles	Strong positive reaction
+++	Erythema, infiltration, confluent vesicles, bullae	Extreme positive reaction
ir	Inflammation sharply limited to the exposed area, lack of infiltrate, small petechiae, pustules, and efflorescences other than papules and vesicles	Irritant reaction
Nt		Not tested

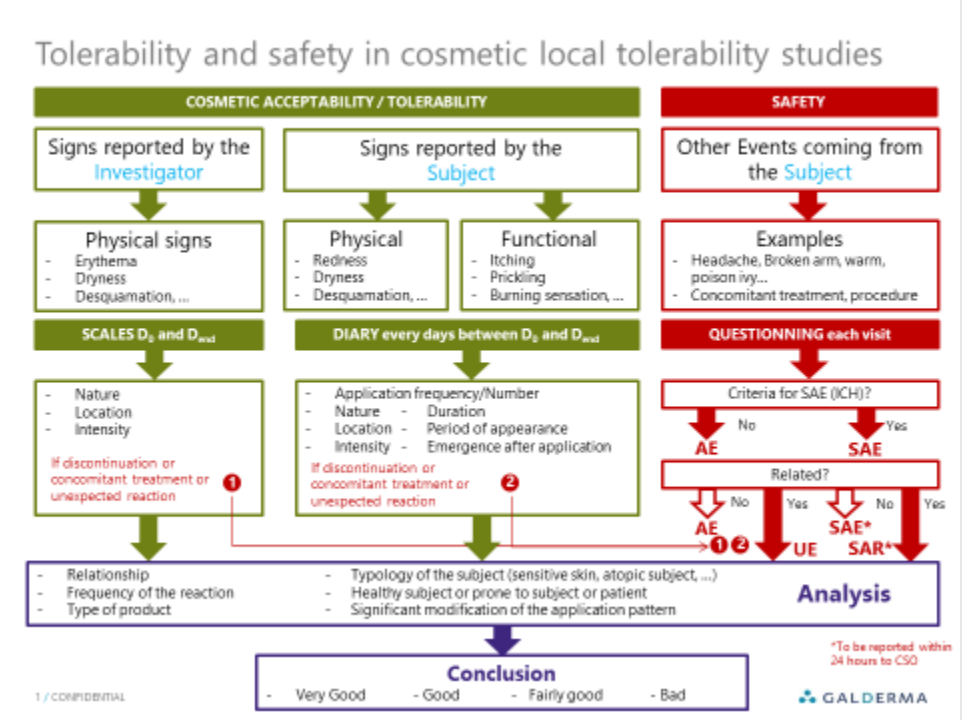
8. At last reading, the investigator will provide an assessment regarding a possible sensitization reaction using the following scale:

Sensitization Reaction	
0	Negative (absence of reaction or might be irritative reaction)
1	Equivocal
2	Positive

9. Report the results from the re-challenge test as directed by the Sponsor and document with photographs.

10. In case of absence of reaction after quotation with the ICDRG scale, the subject may resume product application, if appropriate.

11. After quotation with the ICDRG scale, if the re-challenge is positive, equivocal or in favour of an irritation, notify the Sponsor immediately. Except specific situations, a new series of patch test will be initiated as directed by the Sponsor (with individual ingredients at different concentrations and possibly negative and positive controls) after a minimum of additional two weeks (but not later than 6 months) and after all signs and symptoms have resolved. The patch tests will be placed on a back skin site (or the inner forearm if more appropriate) distant from the site of re-challenge test (e.g. at the left upper back skin if the re-challenge test was done on the right). Follow the same procedure for the patch test as for the re-challenge.



13. ETHICAL AND REGULATORY PROCEDURES

13.1 Research Standards/Good Clinical Practice

This study will be conducted in accordance with all applicable guidelines for the protection of human subjects for research as outlined in 21 CFR 50 the accepted standards for Good Clinical Practice (GCP), and the standard practices of SGS Stephens in accordance with the protocol and amendment(s) as applicable.

13.2 Quality Assurance/Audit/Inspection

To ensure compliance with GCP and all applicable regulatory requirements, Galderma Laboratories, L.P. may conduct a quality assurance audit of the site records, and the regulatory agencies may conduct a regulatory inspection at any time during or after completion of the study. The investigator must agree to grant the auditor(s) and inspector(s) direct access to all relevant documents and to allocate their time and the time of their staff to discuss any findings/relevant issues.

13.3 Institutional Review Board

This study (protocol, ICF and all addenda) will be reviewed and approved by Sterling IRB. The study will not be activated and subjects will not be consented, receive any study products, or participate in any study procedures until the IRB has approved the protocol and the ICF. In addition, the IRB will review the study before any significant change in the protocol is initiated. After each review, the IRB's approval will be documented in a letter to the Investigator and a copy of the IRB approval letter will be forwarded to the Sponsor.

14. STUDY CONDUCT CONDISERATIONS

14.1 Clinical Monitoring

The conduct of the study will be closely monitored by representatives of Galderma Laboratories, L.P. following GCP, ICH guidelines, applicable SOPs, guidelines, and all local regulations. The clinical investigation will be monitored to ensure that: the rights and well-being of the subjects are protected; the reported data are accurate, complete and verifiable from applicable source documents; and the study is conducted in accordance with the currently approved protocol and any other study agreements, GCP, and all applicable regulatory requirements. The investigator will allow the Galderma Laboratories, L.P. representatives to have access to all study records, CRF/eCRFs, corresponding subject medical records, and any other documents considered source documentation. The investigator also agrees to assist the representatives, if required, which can include AE reporting. All study monitoring details will be detailed in the Clinical Monitoring Plan.

14.2 Data Collection

Investigators must keep accurate records of all subjects' visits and all procedures done, being sure to include all pertinent study related information from which CRF/eCRF data will be recorded. Data for this study may be recorded in the subject's chart (e.g. source documents / electronic records) or if approved by the Galderma Laboratories, L.P. directly into CRF/eCRFs. If electronic records are maintained, the method of verification must be determined in advance of starting the study. The process of administering the informed consent must also be documented. Any and all side effects and AEs with the concomitant therapies associated must

be thoroughly documented. Results of any diagnostic tests conducted during the study should be included in the source documentation. Pertinent telephone conversations with the subjects and/or Galderma Laboratories, L.P. concerning the study will be documented and kept on file.

It is required that the author of an entry in the source documents be identifiable. Direct access to all source documentation (medical records) must be allowed for the purpose of verifying that the data recorded in the CRF/eCRF are consistent with the original source.

Only designated individuals may complete the CRF/eCRFs. The principal investigator will review the reported data and certify that the CRF/eCRFs are accurate and complete.

After monitoring has occurred at the clinical site(s) and the CRF/eCRFs have been reviewed, additional data clarifications and/or additions may be needed including AE reporting. Data clarifications and/or additions are documented and are part of each subject's CRF/eCRFs.

14.3 Record Retention

The investigator is required to maintain up-to-date, complete regulatory documentation as indicated by Galderma Laboratories, L.P. and the investigator's files will be reviewed as part of the ongoing study monitoring. The records must be easily accessible when needed (e.g., for a Galderma Laboratories L.P.'s audit or regulatory inspection) and must be available for review in conjunction with assessment of the facility, supporting systems, and relevant site personnel. Financial information is not subject to regulatory inspection and should be kept separately.

Galderma Laboratories, L.P. will inform the investigator of the time period for retaining the site records in order to comply with all applicable regulatory requirements. The minimum retention time will meet the strictest standard applicable to a particular site, as dictated by local laws/regulations, Galderma Laboratories, L.P. SOPs, and/or institutional requirements.

The investigator should take measures to prevent accidental or premature destruction of these documents. If the investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. Galderma Laboratories, L.P. must be notified in writing of the name and address of the new custodian.

14.4 Changes in Study Conduct/Amendments

No amendment will be done for modification(s) due to change in logistical or administrative aspect of the study (e.g., change in monitors, change of telephone numbers). In such a case, the appropriate institution(s) and/or person(s) will be notified of the changes.

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments will be created by Galderma Laboratories, L.P. and must be approved by the IRB prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

Amendments may necessitate that the informed consent and other study-related material be revised. If the consent form is revised, all Subjects/subjects currently enrolled in the study may be required by the IRB to sign the approved, revised informed consent form.

14.5 Confidentiality

All the data provided to the investigator and his/her staff and all data obtained through this Galderma Laboratories, L.P. protocol will be regarded as confidential and proprietary in nature

and should not be disclosed to any third party without Galderma Laboratories, L.P.'s written consent"

15. REFERENCES

1. Doughty, D. Dressings and more: guidelines for topical wound management. *Nurs Clin North Am*. 2005;40:217-31.
2. Ross JI, Snelling AM, Carnegie E, et al. Antibiotic-resistant acne: lessons from Europe. *Br J Dermatol*. 2003;148:467-78.
3. Gehrig KA, Warshaw EM. Allergic contact dermatitis to topical antibiotics: epidemiology, responsible allergens, and management. *J Am Acad Dermatol*. 2008;58:1-21.
4. Trookman NS, Rizer RL, Weber T. Treatment of minor wounds from dermatologic procedures: a comparison of three topical wound care ointments using a laser wound model. *J Am Acad Dermatol*. 2011;64(3 Suppl):S8-S15.

APPENDIX I: INGREDIENT LIST

HEALING OINTMENT

Active ingredient:

Petrolatum 71.5%

Inactive ingredients:

Cetearyl Ethylhexanoate
Butyrospermum Parkii (Shea) Butter
Beeswax
Microcrystalline Wax
Tocopheryl Acetate (Vitamin E Acetate)

APPENDIX II: SELF-ASSESSMENT QUESTIONNAIRE

Day 7/14	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
My wound feels moisturized					
This product soothes the wound and surrounding skin					
I have noticed an improvement in my wound					
This product leaves the wound feeling pleasant					
This product does not irritate the wound area					

Day 28	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
This product does not feel greasy on the skin					
This product provides a protective layer for my wound					
This product keeps the wound surface clean and moisturized					
This product helps heal the wound effectively					
My wound is much improved since using this product					

	Yes	No
I would recommend this product for post-surgical wound care		
I would purchase this product for post-surgical wound care		
I would prefer this product over my previous ointment or petrolatum based-product (for those who used ointment or petrolatum based-product only)		

Testimonials (please provide any comments on the study product, your experience, satisfaction/dissatisfaction, or anything related to this study)

_____

_____